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Hepatitis C Virus Antibody Positivity and Predictors Among Previously Undiagnosed Adult Primary Care Outpatients: Cross-Sectional Analysis of a Multisite Retrospective Cohort Study

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Abstract

Background—Hepatitis C virus (HCV) testing guidance issued by the Centers for Disease Control and Prevention in 1998 recommends HCV antibody (anti-HCV) testing for persons with specified risk factors. The purpose of this study was to determine the prevalence and predictors of anti-HCV positivity among primary care outpatients and estimate the proportion of unidentified anti-HCV-positive (anti-HCV$^+$) persons using risk-based testing.

Methods—We analyzed electronic medical record data from a 4-site retrospective study. Patients were aged ≥18 years, utilized ≥1 outpatient primary care service(s) between 2005 and 2010, and had no documented evidence of prior HCV diagnosis. Among persons tested for anti-HCV, we fit a multilevel logistic regression model to identify patient-level independent predictors of anti-HCV

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Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online (http://cid.oxfordjournals.org). Supplementary materials consist of data provided by the author that are published to benefit the reader. The posted materials are not copyedited. The contents of all supplementary data are the sole responsibility of the authors. Questions or messages regarding errors should be addressed to the author.

Notes

Disclaimer. The findings and conclusions in this report are those of the author(s) and do not necessarily represent the official position of the Centers for Disease Control and Prevention (CDC).

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positivity. We estimated the proportion of unidentified anti-HCV$^+$ persons by using multiple imputation to assign anti-HCV results to untested patients.

Results—We observed 209 076 patients for a median of 5 months (interquartile range, 1–23 months). Among 17 464 (8.4%) patients who were tested for anti-HCV, 6.4% (n = 1115) were positive. We identified history of injection drug use (adjusted odds ratio [95% confidence interval], 6.3 [5.2–7.6]), 1945–1965 birth cohort (4.4 [3.8–5.1]), and elevated alanine aminotransferase levels (4.8 [4.2–5.6]) as independently associated with anti-HCV positivity. We estimated that 81.5% (n = 4890/6005) of anti-HCV$^+$ patients were unidentified using risk-based testing.

Conclusions—In these outpatient primary care settings, risk-based testing may have missed 4 of 5 newly enrolled patients who are anti-HCV$^+$. Without knowing their status, unidentified anti-HCV$^+$ persons cannot receive further clinical evaluation or antiviral treatment, and are unlikely to benefit from secondary prevention recommendations to limit disease progression and mortality.

Keywords

hepatitis C virus (HCV); anti-HCV prevalence; predictors of HCV positivity; outpatient primary care; HCV testing

Hepatitis C virus (HCV) infection is an urgent health problem, with an estimated 4 million persons ever infected and approximately 3 million chronically infected in the United States [1,2].It is estimated that 45%–60% of adults with HCV infection will develop cirrhosis over the next 2–5 decades [3, 4]. In 2010, HCV infection was the underlying or contributing cause of >16 500 deaths in the United States [5].Advances in antiviral therapy have resulted in the potential for dramatic reductions in morbidity and mortality among persons treated for HCV infection [6–9], but care and treatment can only be provided to those infected persons who are tested and identified.

In 1998, Centers for Disease Control and Prevention (CDC) recommended routine HCV antibody (anti-HCV) testing for persons with specified risk factors and medical indications including history of injection drug use (IDU), persistently elevated alanine aminotransferase (ALT) levels, blood transfusion or organ transplant before 1992, clotting factor concentrates before 1987, and long-term hemodialysis [10]; in 1999, the US Public Health Service and the Infectious Diseases Society of America jointly recommended HCV testing for all human immunodeficiency virus (HIV)-infected adults [11]. Several noninterventional studies have since examined the effectiveness of risk-based testing among persons receiving care in clinical settings or persons with access to healthcare; the studies have compared the overall observed anti-HCV prevalence—defined as the number of identified persons divided by the total population of patients (tested and not)— to the expected prevalence as determined by population surveys or modeling [12–15]. Among patients enrolled in an urban managed care organization, Roblin et al determined that the overall observed anti-HCV prevalence was 0.2% [12]; using a population of patients enrolled in 4 private healthcare organizations, Spradling et al found an overall observed prevalence of approximately 0.9% [13]; other researchers have found higher observed prevalence rates ranging from 2.5% to 4.6% among predominantly African American and Hispanic populations receiving routine care in urban primary care settings [14, 15]. Unanimously, the overall observed anti-HCV prevalence in

these settings has been described as lower than expected and the proportion of unidentified anti-HCV positive persons has been estimated as ranging from 40% to 85% [12–16].

In 2012, CDC augmented the risk factor– and medical indication–based HCV screening strategies by issuing a recommendation to test all persons born during 1945–1965 without prior risk ascertainment [17]. Persons in this cohort account for an estimated three-quarters of all HCV infections and HCV-associated deaths in the United States [18, 19]. In 2013, the US Preventive Services Task Force also revised its recommendations to include this birth cohort based on their review of the available evidence [20].

This study sought to determine anti-HCV prevalence and factors associated with anti-HCV positivity in a large geographically and demographically diverse cohort of adult primary care outpatients with no previous diagnosis of HCV. We also aimed to estimate the proportion of unidentified anti-HCV-positive (anti-HCV^{+}) persons within this cohort.

METHODS

Study Design

We conducted a cross-sectional analysis using electronic medical record (EMR) data of patients from the Birth Cohort Evaluation to Advance Screening and Testing for HCV (BEST-C), a multisite retrospective cohort study.

Study Setting and Participants

Participants in BEST-C included all newly enrolled patients aged ≥18 years with no previous diagnosis of anti-HCV who utilized at least 1 primary care outpatient service in 4 large healthcare centers (sites): Mount Sinai Medical Center (MSMC); University of Alabama at Birmingham (UAB); University of Texas, Houston (UTH); and Henry Ford Hospital System (HFH). The study spans 6 years from January 2005 to December 2010 (MSMC, UAB, UTH) or from March 2005 to March 2011 (HFH). Participants with missing values for date of first encounter were excluded.

Only new patients with a first-time encounter through primary care were included in this study based on the understanding that health screening is most likely to occur for new patients [16]; patients with documentation of HCV diagnosis at the time of first encounter were excluded. Data on patient demographics, clinical characteristics, and anti-HCV testing were collected at each patient's first visit and at successive encounters during the study period to create an encounter-level dataset. Encounter-level data were summarized to create a patient-level dataset. The current analysis is based on 209 076 patients. We calculated the period of observation (in months) as the date of last visit minus date of first visit; patients with a single visit were coded as observed for 1 month.

Outcome Variables

The main outcome measure for this analysis was anti-HCV positivity. We defined anti-HCV positivity as a positive test result for antibodies to HCV by enzyme-linked immunoassay at any visit during the study period.

Independent Variables

Independent variables previously associated with anti-HCV positivity were selected for this analysis [12, 14, 21]. Demographic variables examined included birth year, race/ethnicity, sex, marital status, and annual census tract–level income. Census tract income was used as a proxy for household income, which was unavailable. Birth year was dichotomized as *born during 1945–1965* or *born outside the 1945–1965 birth cohort*. Race/ethnicity was categorized as *white*, *black*, *Hispanic*, *Asian*, or *other*. Sex was classified as *male* or *female*. Marital status was categorized as *married*, *divorced/separated/widowed*, or *never married*. Income was categorized as <*$30 000*, *$30 000–$49 999*, *$50 000–$69 000*, *$70 000–$99 000*, and ≥*$100 000*. We also examined the following clinical variables: history of IDU, elevated ALT, hemophilia, HIV infection, and total number of patient encounters with health system during the study period. History of IDU was defined as having an *International Classification of Diseases, Ninth Revision, Clinical Modification* (*ICD-9-CM*) diagnosis code for IDU (292, 304, 305, 969.7, 970.8, 965.01) documented in the EMR at any time during the study period. This search strategy was augmented by text query of the EMR for evidence of IDU. Patients were coded as having a history of elevated ALT if a laboratory record for ALT test with abnormal result was associated with the EMR at any visit during the study period. Cutoff levels used to establish elevated ALT were sex- and site-specific. Hemophilia (*ICD-9-CM* 286.52, 286.5) and HIV infection (*ICD-9-CM* V08, 042) were similarly identified. Identification of HIV infection was enhanced by search of text notes in the EMR. Data regarding other known covariates of anti-HCV positivity such as hemodialysis and blood transfusion before 1992 were not included in this analysis due to lack of consistency in data collection across sites. History of IDU, hemophilia, HIV infection, and elevated ALT were coded as *yes* or *no/unknown*.

Statistical Analysis

Multiple Imputation of Missing Data—Overall, about 51.0% of all patients had missing data for at least 1 demographic variable. To maintain statistical power and to avoid potential bias in statistical estimates [22], we used IVE-ware version 0.1 to replace missing values by multiple imputation using the method of sequential regression multivariate imputation [23]. Imputed datasets were individually analyzed with standard software and summarized per the Rubin method with appropriate adjustment for degrees of freedom [24] (Supplementary Appendix).

Statistical Estimates—Statistical significance for all tests was set at a 2-tailed *P* value of .05. We calculated proportions to describe the characteristics of the overall study population as well as the subpopulation of patients who were tested for anti-HCV at any time during the study period. Overall observed prevalence [13, 14] was estimated by dividing the total number of anti-HCV$^+$ persons by the total number of all participants (tested or not). This approach assumes that because testing is driven by risk factors and medical conditions, patients who are not tested are more likely to be negative for anti-HCV. Expected prevalence was estimated by extending multiple imputation to anti-HCV status for patients who were not tested (Supplementary Appendix). Specifically, imputed anti-HCV values were assigned to each patient who was not tested, fully conditional on all data observed for that patient. The proportion of unidentified anti-HCV$^+$ persons was

subsequently estimated as the difference between expected prevalence and observed prevalence divided by expected prevalence in the study population. We performed sensitivity analyses to assess effect of duration of follow-up on this estimate.

Among patients who were tested for anti-HCV during the 6-year study period, we calculated anti-HCV positivity by dividing the total number of anti-HCV$^+$ patients by the total number of tested patients. To account for clustering of patients within study sites, we used univariate generalized linear mixed models to test for differences in anti-HCV positivity by patient characteristics [25]. We also fit a prespecified multilevel multiple logistic regression model adjusting for the random effect of site to identify independent correlates of anti-HCV positivity among patients tested. The dependent variable was anti-HCV positivity. Patient-level independent variables included the following: birth year, sex, race/ethnicity, marital status, elevated ALT, IDU, hemophilia, HIV status, and total number of visits. Study site was modeled as a second-level random intercept. Census tract income was not included in this model as the variable was not measured at either the site level or the patient level. Sensitivity analysis was performed by comparing estimates from the multiply imputed data to results of complete case analysis. Unless otherwise indicated, we used SU-DAAN (version 10.0.1) and SAS (version 9.3) software to analyze data.

RESULTS

Characteristics of Study Population

A total of 209 076 patients were included in the analysis. The median length of observation was 5 months with an interquartile range of 1 to 23. A summary of the demographic and clinical characteristics of patients is presented in Table 1.

Observed and Expected Prevalence Estimates

The overall observed prevalence (ie, the rate of anti-HCV identification) among all patients was 0.53% (n = 1115/209 076). Using multiply imputed anti-HCV values for patients who were not tested, we estimated the corresponding expected prevalence to be 2.87% (n = 6005/209 076), with a range of 0.84% to 4.34% across the 4 sites. We further estimated that 81.5% (n = 4890/6005) of anti-HCV$^+$ persons were not identified using risk-based testing strategy (Table 2). Upon restricting the analytic data to new patients who had been enrolled in the health system for at least 12 months (median follow-up = 30 months), the proportion of unidentified anti-HCV patients was estimated at 80%; a restricted analysis of new patients who were enrolled for at least 24 months (median follow-up = 40 months) yielded a similar result (79%). Among patients born between 1945 and 1965, the estimated proportion of unidentified anti-HCV$^+$ persons was 76% (ie, observed prevalence = 1.2%; expected prevalence = 4.9%).

Positivity Among Patients Tested

Among patients who were tested for anti-HCV, 6.4% (n = 1115/17 464) were positive (Table 3). About 75% of all anti-HCV$^+$ persons were born during 1945–1965. Anti-HCV positivity was significantly higher in patients born from 1945 to 1965 (13.8%) compared with the referent group of those born before 1945 or after 1965 (2.5%); blacks (12.1%) or Hispanics

(8.5%) relative to whites (5.0%); widowed/divorced/separated (10.4%) or never married (6.7%) compared with married (5.0%); and males (8.8%) vs females (4.4%) (Table 3). Anti-HCV positivity was also greater in patients with a history of elevated ALT (14.9%), IDU (35.8%), hemophilia (10.7%), or HIV (17.3%).

Predictors of Anti-HCV Positivity Among Patients Tested

Following multivariate adjustment in a multilevel logistic regression model, we identified IDU (adjusted odds ratio [AOR], 6.3 [95% confidence interval {CI}, 5.2–7.6]), 1945–1965 birth cohort (AOR, 4.4 [95% CI, 3.8–5.1]), elevated ALT (AOR, 4.8 [95% CI, 4.2–5.6]), black race (AOR, 1.9 [95% CI, 1.6–2.2]), Hispanic ethnicity (AOR, 1.5 [95% CI, 1.2–2.0]), widowed/divorced/separated (AOR, 1.5 [95% CI, 1.2–2.0]), never married (AOR, 1.4 [95% CI, 1.2–1.6]), and male sex (AOR, 1.3 [95% CI, 1.2–1.6]) as significant correlates of anti-HCV positivity (Table 4). Hemophilia and HIV-positive status were not significantly associated with anti-HCV positivity. Sensitivity analysis using complete cases indicated that point estimates were comparable to results from the imputed data, imputation restored statistical efficiency and produced estimates with better precision (Table 5).

DISCUSSION

This is a multisite study in the United States examining anti-HCV positivity in a large cohort of newly enrolled, previously undiagnosed adult primary care outpatients from different regions of the country. We found that over a 6-year period, 6.4% of tested patients were anti-HCV$^+$. However, as the majority of patients were not tested, the observed prevalence was just above 0.5%. We estimated that the expected anti-HCV prevalence in this population could be as high as 2.9%, indicating that during the study period, >81% of anti-HCV$^+$ persons may have been undetected.

The findings from this study are supported by previous research. Anti-HCV positivity among patients tested and the observed prevalence are comparable to results from Spradling et al, who used a similarly diverse population of patients with access to care: estimates for anti-HCV prevalence among patients tested and observed are 5.5% and 0.7%, respectively, when the data are restricted to patients with no history of HCV diagnosis [13]. Roblin et al also reported an anti-HCV positivity of 5.1% among patients tested and an overall observed prevalence of 0.2%, although the proportion of patients tested was considerably lower [12]. Southern et al [14] found a much higher prevalence of anti-HCV among patients tested (11.5%) and overall observed prevalence (4.6%), likely reflecting a higher local prevalence of HCV and HCV risk factors [26, 27] and a higher-than-average proportion of patients tested for anti-HCV of nearly 40% [14]. Our expected prevalence estimate can be reasonably compared to an estimate of 2.0% anti-HCV prevalence among US adults aged 20–70 years [18], accounting for the fact that African Americans, a high-prevalence group, are substantially overrepresented in the outpatient primary care cohort used for the current study. Moreover, our finding that testing based on risks or medical indications in the clinical setting underestimates anti-HCV prevalence by 81% is within the range of earlier findings [12–14]. Notably, our data further suggest that anti-HCV prevalence may vary regionally in

the United States (Table 2). This observation is supported by prevalence estimates from prior studies [14, 26, 28, 29].

Our analysis also indicated that patients' birth year, history of IDU, and elevated ALT were significant correlates of anti-HCV positivity, as were black race, Hispanic ethnicity, single marital status, and male sex. History of IDU and elevated ALT as predictors of anti-HCV positivity are consistent with the data supporting risk-based testing recommendations [12, 14, 15, 30]. Race, ethnicity, sex, and marital status have also previously been associated with anti-HCV positivity or current HCV infection [1, 13, 14]. Nevertheless, the finding that 74% of the identified anti-HCV$^+$ patients were born from 1945 to 1965 provides additional data in support of recommendations by the CDC and the US Preventive Task Force [17, 20] for HCV testing in this birth cohort and confirms previous findings of the burden of prevalence in this cohort [13, 14, 19, 21].

This study has several strengths. The analysis of a large, demographically diverse, multisite, multiyear cohort of outpatient primary care patients representing different geographic regions of the country increases the potential generalizability of the findings. Also, the use of multilevel modeling to adjust for correlation between patients within sites (healthcare centers) ensures that standard error estimates are conservative. Moreover, the use of multiple imputation to replace missing data restored statistical power and improved precision of estimates.

However, there are also some important limitations. First, blood transfusion before 1992, an important determinant of anti-HCV positivity among older adults, was not included in this analysis due to a lack of consistent data collection across sites. Second, it is likely that risk factors such as IDU were underreported [31–35]; nondisclosure of relevant patient risk factors could lead to confounding of estimates [36]. Nonetheless, we determined that the proportions of patients identified as having history of IDU, hemophilia, HIV positivity, or elevated ALT were comparable to estimates reported in previous studies [12, 14, 16]. Third, cross-sectional analysis of this dataset limits our ability to assess temporal associations between independent risk factors and anti-HCV positivity; however, cross-sectional analysis was appropriate for other important objectives in this study such as estimates of anti-HCV prevalence and proportion of unidentified anti-HCV$^+$ persons. Fourth, it is likely that retrospective review of EMR did not adequately identify patients diagnosed with HCV outside participating health systems prior to their first encounter; patients with a previous HCV diagnosis who were misclassified at the first encounter would have been included in the study and may not have received additional HCV testing during the study. In addition, we were unable to identify patients diagnosed outside participating health systems during the study, and our estimate of unidentified anti-HCV$^+$ persons may be inflated as a result. Finally, in using multiple imputation to assign plausible values to missing data (sex, race/ethnicity, marital status, expected anti-HCV prevalence), we assumed that missing values were missing at random (eg, missing data values for sex or anti-HCV status are related conditionally to observed patient characteristics) [22, 23]. Despite our efforts to make this assumption more plausible [25, 37] by including a large number of relevant predictors in the imputation models, the assumption may not be fully met because there is a good likelihood that not all patient variables were observed. Still, others have noted that missing data

originating from medical research are often related to observed patient data and that the missing-at-random assumption may be appropriate [22,38].

Despite these limitations, our findings demonstrate that testing based on risk and medical indications alone failed to identify four-fifths of previously undiagnosed adults with past exposure to HCV. This may be due in part to the difficulty in capturing complete patient risk history (eg, IDU) in EMRs to support the implementation of comprehensive risk–based HCV testing algorithms. HCV-infected persons who are not aware of their status cannot receive further clinical evaluation or antiviral treatment, and are unlikely to benefit from preventive services or secondary prevention recommendations (eg, reduction in alcohol use and other lifestyle changes) aimed at limiting disease progression and reducing liver-related morbidity and mortality [39, 40]. In the routine clinical environment, recent CDC and US Preventive Task Force recommendations to test patients born during 1945–1965 for HCV without the need for prior ascertainment of risk factors should be implemented [17, 20]. With the alignment of the risk-based and birth cohort testing recommendations, it is expected that identification of infected persons who were previously undiagnosed will increase, leading to higher rates of linkage to care and treatment as appropriate, or to programs that support linkage to care and treatment adherence, which would further result in reduced morbidity and mortality associated with HCV.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Characteristics of Study Population

Characteristic	All Patients, No. (%)	Patients Tested, No. (%)
Overall	209 076 (100)	17 464 (100)
Age, y, median (IQR)	37 (28–50)	37 (28–49)
1945–1965 birth cohort	70 718 (33.8)	5989 (34.3)
Female sex[a]	137 695 (65.6)	9706 (45.6)
Race/ethnicity[a]		
White	95 992 (45.9)	6554 (37.5)
Black	58 437 (27.9)	6757 (38.7)
Hispanic	14 526 (6.9)	1065 (6.1)
Asian	9492 (4.5)	909 (5.2)
Other	30 630 (14.7)	2179 (12.5)
Marital status[a]		
Married	94 673 (45.3)	6434 (36.8)
Widowed/divorced	15 866 (7.6)	1582 (9.1)
Never married	98 537 (47.1)	9448 (54.1)
Income category[a]		
<$30 000	34 561 (16.5)	3671 (21.0)
$30 000–$49 999	58 227 (27.8)	5209 (29.8)
$50 000–$69 000	51 440 (18.7)	4215 (24.1)
$70 000–$99 999	39 145 (18.7)	2800 (16.03)
≥$100 000	25 704 (12.3)	1569 (9.0)
Injection drug use	2992 (1.4)	1007 (5.8)
Hemophilia	1241 (0.6)	299 (1.7)
Elevated ALT	12 574 (6.0)	4618 (26.4)
HIV infected	1240 (0.6)	767 (4.4)

Abbreviations: ALT, alanine aminotransferase; HIV, human immunodeficiency virus; IQR, interquartile range.

[a]Missing values for sex, race/ethnicity, marital status, and income were multiply imputed.

Table 2

Observed and Expected Estimates of Hepatitis C Virus Antibody Prevalence Among Previously Undiagnosed Patients (N = 209 076)

Estimate	All Sites	HFH	MSMC	UAB	UTH
Observed prevalence estimate, % (No.)	0.53 (1115)	0.6 (601)	0.85 (315)	0.18 (72)	0.39 (127)
Expected prevalence estimate, % (No.)	2.87 (6005)	2.84 (2830)	3.82 (1423)	0.83 (328)	4.33 (1424)
Estimated unidentified persons, % (No.)	81.5 (4890)	78.7 (2229)	77.9 (1109)	78.0 (256)	91.1 (1297)

Abbreviations: HFH, Henry Ford Hospital; MSMC, Mt Sinai Medical Center; UAB, University of Alabama at Birmingham; UTH, University of Texas, Houston.

Table 3

Probability of Testing Hepatitis C Virus Antibody Positive, by Demographic and Clinical Characteristics

Characteristic	Patients Tested, No.	Patients Positive, No. (%)	*P* Value*
Overall	17 464	1115 (6.4)	…
1945–1965 birth cohort	286		
No	11 475	286 (2.5)	…
Yes	5989	829 (13.8)	<.0001
Sex[a]			
Female	9706	429 (4.4)	…
Male	7758	686 (8.8)	<.0001
Race/ethnicity[a]			
White	6554	330 (5.0)	…
Black	6757	574 (8.5)	<.0001
Hispanic	1065	129 (12.1)	.0001
Asian	909	16 (1.7)	<.0001
Other	2179	67 (3.1)	.0119
Marital status[a]			
Married	6434	319 (5.0)	…
Widowed/divorced	1582	164 (10.4)	<.0001
Never married	9448	632 (6.7)	.0178
Income category[a]			
<$30 000	3671	366 (10.0)	<.0001
$30 000–$49 999	5209	361 (6.9)	<.0001
$50 000–$69 000	4215	225 (5.3)	.0014
$70 000–$99 999	2800	106 (3.8)	.5743
≥$100 000	1569	57 (3.6)	…
Elevated ALT			
No/unknown	12 846	425 (3.3)	…
Yes	4618	691 (14.9)	.0001
Injection drug use			
No/unknown	16 457	754 (4.6)	…
Yes	1007	365 (35.8)	<.0001
Hemophilia			
No/unknown	17 165	1083 (6.3)	…
Yes	299	32 (10.7)	.0318
HIV infected			
No/unknown	16 697	982 (5.9)	…
Yes	767	133 (17.3)	.0045

Abbreviations: ALT, alanine aminotransferase; HIV, human immunodeficiency virus.

[a] Missing values for sex, race/ethnicity, marital status, and income were multiply imputed.

[*] *P* values obtained from univariate generalized linear mixed model incorporating random effect of site.

Table 4

Model-Adjusted Odds Ratios for Hepatitis C Virus Antibody Positivity

Characteristic (n = 17 464)	Adjusted[a] OR (95% CI)	*P* Value
1945–1965 birth cohort		
No	1.0	…
Yes	4.4 (3.8–5.1)	<.0001
Sex[b]		
Female	1.0	…
Male	1.4 (1.2–1.6)	<.0001
Race/ethnicity[b]		
White	1.0	…
Black	1.9 (1.6–2.2)	<.0001
Hispanic	1.5 (1.2–2.0)	.0022
Asian	0.6 (.4–1.1)	.0874
Other	1.1 (.8–1.5)	.4142
Marital status[b]		
Married	1.0	…
Widowed/divorced	1.5 (1.2–2.0)	.0019
Never married	1.4 (1.2–1.6)	.0003
Elevated ALT		
No/unknown	1.0	…
Yes	4.8 (4.2–5.6)	<.0001
Injection drug use		
No/unknown	1.0	…
Yes	6.3 (5.2–7.6)	<.0001
Hemophilia		
No/unknown	1.0	…
Yes	1.1 (.7–1.7)	.6207
HIV infected		
No/unknown	1.0	…
Yes	1.0 (.8–1.3)	.7571

Abbreviations: ALT, alanine aminotransferase; CI, confidence interval; HIV, human immunodeficiency virus; OR, odds ratio.

[a] Multilevel model adjusted for random effect of site and the following individual-level fixed effects: birth year, sex, race, marital status, injection drug use, elevated ALT, hemophilia, HIV status, and total number of encounters with healthcare system.

[b] Missing values for sex, race/ethnicity, and marital status were multiply imputed.

Table 5

Comparison Between Estimates From Multiply Imputed and Complete Case Analytic Models for Hepatitis C Virus Antibody Positivity

	Adjusted[a] OR (95% CI)	
Characteristic	**Multiply Imputed[b] (n = 17 464)**	**Complete Case (n = 13 689)**
1945–1965 birth cohort		
No	1.0	1.0
Yes	4.4 (3.8–5.1) *	4.2 (3.2–5.5) *
Sex		
Female	1.0	1.0
Male	1.4 (1.2–1.6) *	1.3 (1.0–1.6)
Race/ethnicity		
White	1.0	1.0
Black	1.9 (1.6–2.2) *	1.8 (1.5–2.2) *
Hispanic	1.5 (1.2–2.0) **	1.5 (1.1 –2.2) ***
Asian	0.6 (.4–1.1)	0.6 (.3–1.2)
Other	1.1 (.8–1.5)	1.2 (.8–1.7)
Marital status		
Married	1.0	1.0
Divorced/widowed	1.5 (1.2–2.0) **	1.5 (1.1 –2.0) ***
Never married	1.4 (1.2–1.6) *	1.4(1.1–1.7) ***
Elevated ALT		
No/unknown	1.0	1.0
Yes	4.8 (4.2–5.6) *	4.8 (3.7–6.2) *
Injection drug use		
No/unknown	1.0	1.0
Yes	6.3 (5.2–7.6) *	6.4 (4.6–8.9) *
Hemophilia		
No/unknown	1.0	1.0
Yes	1.1 (.7–1.7)	1.0 (.5–2.2)
HIV infected		
No/unknown	1.0	1.0
Yes	1.0 (.8–1.3)	1.0 (.6–1.6)

Abbreviations: ALT, alanine aminotransferase; CI, confidence interval; HIV, human immunodeficiency virus; OR, odds ratio.

[a] Adjusted for random effect of site and the following fixed effects: birth year, sex, race, marital status, injection drug use, elevated ALT, hemophilia, HIV status, and total number of encounters with healthcare system.

[b] Missing values for sex, race/ethnicity, and marital status were multiply imputed.

*$P < .001$.

**P values were between <.001 and <.01.

***P values were between <.01 and <.05.